REMARKS

Favorable reconsideration is respectfully requested in view of the remarks of record and the following remarks.

On pages 2-5 of the Office Action, claims 1-4 and 9-11 were rejected under 35 U.S.C. § 103(a) as obvious over Graham (1984), Fu et al., and Chen et al. or Snaith et al., in light of Graham et al.

Applicants respectfully traverse this rejection for the reasons of record and for the following reasons.

The cited art references fail to teach each and every element of the claimed invention, and they fail to teach or suggest the increased efficiency of the claimed invention.

As noted previously, the specification (at page 3, last paragraph, to page 4, second paragraph) describes Graham (1984). In particular, this reference discloses a method for constructing a recombinant adenovirus vector using a circular DNA constructed by inserting a small plasmid at the restriction enzyme Xba I site, which exists at one location in the E1 region of the adenovirus 5 type, and then transfecting this vector into a mammalian cell line (293 cells). Graham reported that such circular DNA produces infectious virus. See also the Abstract on page 2917 of Graham (1984). Thus, Graham (1984) suggests that a recombinant adenovirus vector can be constructed by replacing the E1 region or E3 region of a circular adenovirus DNA with an exogenous gene.

However, the method in Graham (1984) differs from that of the instant invention in that when a recombinant adenovirus vector is actually constructed using the method in Graham (1984), two problems arise. First is the problem of low efficiency in incorporating the expression cassette into the extremely large plasmid which contains the adenovirus genome DNA. Second, the plasmid DNA portions remain in the constructed adenovirus vector. See page 4, lines 6-12 of the disclosure.

The Applicants were the first to recognize and solve these problems with the present invention. The method of the present invention does not have a low efficiency of incorporating the expression cassette and it deletes the cosmid vector. The deletion of the cosmid sequence

means that the resultant recombinant adenovirus vector does not retain the plasmid DNA portions as in Graham (1984). Thus, the method of the present invention results in a ***structurally different*** recombinant adenovirus vector from that in Graham (1984). Therefore, Graham (1984) does not teach the present invention as essentially claimed.

On the other hand, Fu et al. discloses a "cosmid adenoviral cloning system', to which a 6-8 kb expression cassette can be cloned in order to form a 38 kb vector. 38 kb is the largest size of adenovirus to be transfected into cells. However, this cosmid adenoviral cloning system of Fu et al. contains cosmid sequence (COS-ITR) in the resultant vector. This is clearly different from the present invention which removes the cosmid sequence. This difference affects the generation efficiency of infectious adenoviral plaques.

Fu et al. describes that the cosmid adenoviral cloning method generated two infectious AdCGALCOS adenoviral plaques out of five Petri dishes (page 1328, right column, lines 2-4). From Table 1 of Fu et al., it is apparent that 10 μg of DNA (i.e., recombinant adenovirus vector, AdCGALCOS) was added per dish. That is, two adenoviral plaques are generated from a total of 50 μg of transfected DNA (page 1328, right column, lines 4-5). On the other hand, in the present invention, 1 μg of pALC-IL-5 (i.e., a recombinant adenoviral vector) was added into each well of a 12-well plate, and plaques were generated in each well (Example 3). This means that, if at least one plaque was generated per well, 12 plaques were generated from a total of 12 μg of transfected DNA. Thus, the efficiency in Fu et al. was 2 plaques/50 μg of DNA, while the present invention has an efficiency of 12 plaques/12 μg DNA. This difference in efficiency is important for preparing recombinant adenovirus for gene therapy.

Applicants further note Fu et al. does not teach or suggest the significance of complete removal of cosmid sequence.

Further, neither Chen et al. nor Snaith et al. teach or suggest the improved efficiency of the claimed invention.

Therefore, for the above-noted reasons, this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing remarks, the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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